HHS Public Access

Author manuscript

Curr Fungal Infect Rep. Author manuscript; available in PMC 2015 October 30.

Published in final edited form as:

Curr Fungal Infect Rep. 2012 September ; 6(3): 170–177. doi:10.1007/s12281-012-0094-x.

Recent Taxonomic Developments with *Candida* and Other Opportunistic Yeasts

Mary E. Brandt and **Shawn R. Lockhart**

Mycotic Diseases Branch, Centers for Disease Control and Prevention, 1600 Clifton Road; Mailstop G-11, Atlanta, GA 30333, USA

Mary E. Brandt: mbb4@cdc.gov; Shawn R. Lockhart: gyi2@cdc.gov

Abstract

Increases in susceptible patient populations and advances in identification methods have resulted in the continued recognition of novel yeasts as agents of human infection. Most of these agents are members of the well-recognized genera *Candida*, *Cryptococcus*, *Trichosporon*, and *Rhodotorula*. Some of these agents are "cryptic species," members of species complexes, and may not be detectable using classical carbohydrate assimilation-based methods of yeast identification. Such species require DNA- or MALDI-based methods for correct identification, although sporadic isolates may not routinely require delineation to the individual species level. The coming end of the fungal taxonomy rules requiring separate names for sexual and asexual forms of the same fungus will hopefully allow greater clarity, as names for medically important yeast can now be based on the needs of the medical mycology community and the common goal of better communication between laboratory and clinician.

Keywords

Non-*albicans Candida*; *Candida* species; *Cryptococcus* species; *Trichosporon* species; Emerging fungal infections; Antifungal resistance; Yeast infection

Introduction

Recent developments in medical mycology have revolutionized the detection, identification and treatment of fungal infections. The proven utility of DNA sequencing has enabled the identification of fungal organisms even when present in formalin-fixed tissue sections, growing poorly, not sporulating, not viable, or otherwise present in less than optimal conditions. MALDI-TOF mass spectrometry [1] and Fourier Transform Infrared spectroscopy (FT-IR) based identification systems are beginning to demonstrate similar levels of sensitivity and specificity with yeasts and some molds. The ability to identify a broader range of fungal isolates and understand their taxonomic placement has allowed targeting of antifungal drugs to specific genera or groups of organisms. Furthermore, the growing use of whole-genome sequencing of clinically important fungal organisms is

Correspondence to: Mary E. Brandt, mbb4@cdc.gov.

Disclosure No potential conflicts of interest relevant to this article were reported.

allowing specific antifungal resistance targets and virulence factors to be described and analyzed in greater detail than before. The overall effects of this research are to predict with greater specificity and accuracy the particular antifungal drugs that would be most useful in treating a particular organism and to identify rapidly those isolates likely to be resistant to various drugs.

The ability to identify organisms based on DNA sequences has contributed to the recognition of “cryptic species” or “species complexes.” These are groups of organisms that are indistinguishable from one another when morphologic or biochemical traits are used for identification, but have distinct DNA sequences at particular target regions that can be used to separate them. Several “cryptic species” have also been recognized as human pathogens, albeit at lower prevalence than their original counterparts. In many cases, the cryptic species have been given formal species names, such as *Candida orthopsilosis* and *C. metapsilosis* within the *Candida parapsilosis* species complex. These findings have led to re-evaluating the definition of a “species,” and we currently use a phylogenetic definition based on the degree of sequence identity (homology) between an unknown isolate and its comparators at particular genetic loci [2••, 3]. However, there are still no hard and fast rules for the degree of concordance necessary for two isolates to be considered “identical” or “different” species [4•].

Another recent taxonomic change that will soon impact the medical mycology community is the end of “one fungus-two names,” the long-established taxonomic rule of requiring separate names to be used for the sexual and asexual forms of a fungus [5••]. For example, the asexual name *Candida kefyr* and the sexual name *Kluyveromyces marxianus* refer to the same organism. This practice has caused confusion in the clinical mycology community for decades, due to difficulty in recognizing that both names describe a single organism. The use of DNA-based phylogenetic methods means that an organism can be named and placed in a taxonomic grouping without having to establish the presence of sexual spores and spore-bearing structures, which had been a prerequisite for assigning a sexual name. For this reason, the “two-name” system rapidly became obsolete, and on July 30, 2011, the XVIII International Botanical Congress decided to end this practice. Although the International Botanical Congress is still formulating rules for the new nomenclature, it appears that the correct name will be the earliest name published according to the rules of legitimacy, and organisms previously designated with two names should have the earliest name considered legitimate and valid. This suggests that in cases when adoption of a sexual (teleomorph) name will cause confusion, asexual (anamorph) names that are well known and commonly used will be adopted and validated. Although it is not clear what will happen to the less common name, this is a very welcome development, as it promotes clear communication between the laboratory and the clinician and allows teaching of one name for each organism. In some cases input will be required from the clinical mycology community to determine the name to be retained.

The purpose of this paper is to review each major genus of medically important yeast from the perspective of recent taxonomic changes and their clinical impacts. This paper will use the commonly accepted names, which are usually the anamorph names, although the teleomorph names will be referred to as appropriate.

Candida and Other Ascomycetous Yeast

This genus contains approximately 200 species, and is the largest genus of medically important yeast. At least 30 *Candida* species have been recognized as causes of human infection, and the list continues to expand [6].

Candida albicans

Candida albicans remains the major pathogen in this group, although its prevalence in blood cultures is being surpassed by the group of non-*albicans* species. A general-purpose genotype (GPG; also known as clade 1) of *C. albicans* has been identified and has been reported to cause more infections than other *C. albicans* genotypes. A recent French study suggests that GPG bloodstream strains have a higher prevalence in younger patients (exceeding 40 % in infants less than one year), and may be more virulent than other strains in younger patients [7].

Candida dubliniensis

Candida dubliniensis is a closely related organism that has many phenotypic similarities to *C. albicans*. Both species display a green color on ChromAgar media, produce germ tubes when incubated with serum, and produce chlamydospores on cornmeal or rice-Tween agars. Pal's (sunflower seed), tobacco, and Niger seed agars have been proposed as methods to distinguish the two species. However none of these phenotypic methods used alone is completely reliable in separating them. In a recent College of American Pathologists proficiency sample (2010-A-F01), 411 (39.4 %) of 1046 participant laboratories correctly identified the challenge isolate as *C. dubliniensis*, while 445 participants (42.6 %) identified the isolate incorrectly as *C. albicans* (CAP final critique F-A survey 2010, College of American Pathologists). The 13 laboratories that used molecular methods all provided the correct identification. The most reliable methods to separate these two species at this time are molecular-based (DNA sequencing, specific DNA probe, MALDI-TOF) [8].

The question of whether it is necessary to separate these two species routinely in the clinical laboratory has recently been addressed [9]. Concern has been expressed that *C. dubliniensis* needs to be identified because resistance to fluconazole is frequently seen. Indeed, many of the first strains of *C. dubliniensis* were recovered from oral samples of HIV-infected patients who were receiving fluconazole for treatment of mucocutaneous candidiasis, and did exhibit elevated MIC values to fluconazole. However, recent investigations of bloodstream and other sterile-site isolates collected in surveillance studies showed that very few of these isolates demonstrated fluconazole resistance as measured by MIC testing. In a CDC study, 2/42 (4.7 %) bloodstream isolates had a value of 16 μg/mL, which is considered resistant with the new CLSI breakpoints. In the ARTEMIS global surveillance, 3.9 % of 310 isolates were resistant to fluconazole. The Denmark national surveillance found 3.1% resistance among 65 isolates [9]. Taken together, these studies show that fluconazole resistance among *C. dubliniensis* remains very low, at less than 5 %. These results suggest that speciation may be necessary for an outbreak investigation or other epidemiologic purposes, but for most sporadic isolates, there is no reason to separate *C. dubliniensis* from *C. albicans* routinely.

MIC testing will likely provide a more direct answer to the assessment of fluconazole resistance in a suspect isolate.

Candida africana

Another organism first described as an atypical *Candida albicans* is *Candida africana*, which has been reported as a cause of vaginitis in African, German, Spanish and Italian patients [reviewed in 10]. The taxonomic position of this organism is still in doubt, and many authors consider it as a biovar of *C. albicans* rather than a distinct species. *C. africana* produces germ tubes in serum but does not produce chlamydospores on corn meal agar. It also appears to be susceptible to commonly used antifungal agents. Sequencing of ribosomal ITS (internal transcribed spacer) and D1–D2 regions shows a high level of sequence homology (>99 %) not sufficient to separate the two taxa. It has been speculated that *C. africana* may have been generated as a result of the parasexual mating cycle reported in *C. albicans*, which can result in extensive genetic recombination between chromosomes and the formation of variant genotypes [10].

Candida parapsilosis

DNA-based methods have been used to recognize two additional cryptic species that have similar morphology: *C. orthopsilosis* and *C. metapsilosis*. *C. parapsilosis* remains as a major opportunistic and nosocomial pathogen that is generally susceptible to antifungal agents, although MIC values to echinocandins are elevated. *C. metapsilosis* and *C. orthopsilosis* are found at low prevalence (~1 %) in most bloodstream isolate collections surveyed [11] and respond well to antifungal agents, so routine identification of these species is probably not necessary. The three species require molecular methods to distinguish them from one another.

Candida glabrata

This species remains one of the most difficult to treat because of its inherent decreased susceptibility to azoles and its ability to acquire azole resistance rapidly. It is more closely related to *Saccharomyces cerevisiae* than to other *Candida* species. The species *Candida bracarensis* and *C. nivariensis* are genetically related to *C. glabrata*. Their prevalence in clinical samples is low, estimated at 1 % to 2 % of isolates identified phenotypically as *C. glabrata*, but both species have been identified as causative agents of invasive infection. *Candida bracarensis* and *C. nivariensis* both display white colonies on ChromAgar, in contrast to the pink colonies of *C. glabrata*. They also show variable ability to assimilate trehalose, with *C. nivariensis* unable to assimilate this substrate, *C. bracarensis* showing variable results, and *C. glabrata* usually able to assimilate trehalose. These three species require DNA sequencing to separate them. *C. nivariensis* is most notable for elevated MIC values to azole agents. *C. bracarensis* is more variable in susceptibility, with both high and low azole MIC values reported [12].

Candida tropicalis

Candida tropicalis has been recognized as an increasing cause of bloodstream infection outside the United States, particularly in South America and Asia. The reasons for its high

prevalence in certain geographic regions of the world are not clear. Although most *C. tropicalis* isolates remain susceptible to antifungals, human isolates with resistance to fluconazole are occasionally reported, most recently from Taiwan [13].

Other Non-*albicans Candida* Species

Candida krusei is the fifth most common cause of candidemia in most surveys. It is well known for its innate resistance to fluconazole and reduced susceptibility to amphotericin B. The teleomorph has recently been moved from *Issatchenkia orientalis* to *Pichia kudriavzevii* [14••]. This species is most closely related genetically to *Pichia* (*Candida*) *norvegensis* and *Candida inconspicua*, both rare causes of human infection.

The newly-named genus *Meyerozyma* includes *Candida guilliermondii* (*Meyerozyma guilliermondii*) and *Candida fermentati* (*Meyerozyma caribbica*). *Candida carpophila* is closely related but with no known teleomorph. The epidemiology of this species complex has been recently reviewed [15]; they are agents of bloodstream and deep tissue infections, although their incidence is low even among immune-compromised hosts (from 1 % in Europe to 3.7 % in Latin America). It is difficult to distinguish accurately among the species in this complex and related species such as *Candida famata* and *Candida haemulonii* using phenotype-based methods due to the great heterogeneity in morphology and carbon assimilation profiles. In fact, *C. guilliermondii* and *C. fermentati* show no differences on standard fermentation and growth tests. Molecular methods are recommended for distinction among these species, but such methods may not be needed for identification of sporadic isolates.

In some studies, 75 % of *C guilliermondii* isolates demonstrated reduced susceptibility to fluconazole, although most isolates are susceptible to azoles [15]. Along with *C. parapsilosis*, this organism is one of the two yeast species with highest MIC values to echinocandin drugs. Most isolates are susceptible to amphotericin B although the species is thought to be polyene-tolerant.

Candida palmioleophila is another yeast species commonly misidentified as *C. famata* or *C. guilliermondii*. It is distinguishable by ITS sequence and MALDI-TOF profile. A recent study in Denmark identified 8 isolates of *C. palmioleophila*, all with high fluconazole MIC values, among bloodstream isolates [16]. This species has no known teleomorph.

Candida rugosa has been reported mostly from Latin America as an emerging fungal pathogen. Other members of this species complex *C. pararugosa* and *C. pseudorugosa* have also been described. A recent DNA sequencing analysis of 24 isolates phenotypically identified as *C. rugosa* showed that 10 isolates were actually *C. rugosa*, while another 10 isolates were identified as *C. pararugosa*, 2 isolates were *C. pseudorugosa*, and two isolates with divergent DNA profiles were named as a novel species *C. neorugosa* [17]. When tested using the CLSI broth microdilution method, all classes of antifungal drugs appeared to show good activity against these four species [17]. A case of bloodstream infection with a novel unnamed species closely related to *C. pseudorugosa* has also been recently described [18]. This organism was reported as resistant to fluconazole and to some echinocandin drugs when tested according to the EUCAST microdilution protocol [18].

Candida kefyr, *Candida norvegensis*, *Candida lusitaniae*, *Candida zeylanoides* and *Candida famata*, among other minor species (see Table 1), cause less than 1 % of bloodstream and other deep infections. These species are noteworthy because occasional antifungal resistant isolates can be detected, and because commercial yeast identification systems may misidentify such isolates in the clinical laboratory. DNA sequencing or MALDI methods are required to identify such isolates when definitive information is required. Some of these species may not be recognized because they are frequently reported using their teleomorph genus names which include *Pichia (Candida norvegensis)*, *Lindnera (Candida utilis*), *Clavispora* (*Candida lusitaniae*), *Debaryomyces* (*Candida famata*), *Kluyveromyces (Candida kefyr)*, *Trichomonoascus* (*Candida ciferrii*), *Yarrowia* (*Candida lipolytica*), and other names that may not be familiar to clinical microbiology personnel (Table 1). Recent taxonomic changes compound this problem. For example, the genus *Pichia* has recently been reassessed and the number of assigned species reduced from over 100 to about 20 [19]. The species that were removed from this genus were assigned to over 20 other genera. A few of these organisms are noteworthy causes of fungal infections. *Pichia anomala* (*Candida pelliculosa*) was reassigned to the newly created genus *Wickerhamomyces* as *Wickerhamomyces anomalus* [19]. Earlier the organism *Pichia ohmeri* (formerly called *Candida guilliermondii* var. *membranifaciens*) was reassigned to the genus *Kodamaea* [20]. The fungus nomenclature database Mycobank now lists three valid names for this organism: *Kodamaea ohmeri*, *Yamadazyma ohmeri*, and *Endomycopsis ohmeri*. It is hoped that the new International Botanical Congress-approved taxonomic changes mentioned above will allow the clinically important species to be known by their anamorph (*Candida*) names. However, the clinical community should be aware of multiple names for these organisms that may appear in the medical literature and should appreciate that, in many cases, these names all refer to a single organism.

Blastoschizomyces capitatus (*Dipodascus capitatus*) is an uncommon cause of disseminated disease in immunosuppressed individuals. An older name for this fungus is *Geotrichum capitatum*. *Geotrichum candidum* has its teleomorph in the genus *Galactomyces* as *G. candidus*. Although these two organisms are not closely genetically related, both produces arthroconidia and can be confused with *Trichosporon* species (see below).

Novel Species with Single Case Reports

Recently the novel species *Candida aaseri* and *C. pseudoaaseri*, which are close genetic relatives, have been recovered from human clinical samples. *C. aaseri* was isolated from sputum of a Norwegian patient and was not considered clinically relevant, but *C. pseudoaaseri* was recovered from blood in an immunocompromised cancer patient in Germany [21]. Both species produce a blue colony on ChromAgar Candida somewhat similar to that of *C tropicalis*, produce pseudohyphae but not chlamydospores on cornmeal agar, and require DNA sequencing to distinguish them, relying on variation in the ITS region. *C. pseudoaaseri* has low MICs to all classes of antifungal drugs except flucytosine, a feature that also distinguishes this species from *C. aaseri*, which is generally susceptible.

Candida subhashii was isolated from peritoneal fluid in a patient with end-stage renal failure and peritonitis [22]. The isolate was white on ChromAgar Candida and produced long

pseudohyphae on cornmeal agar. Identification was made by DNA sequencing, where the isolate was found to be genetically most closely related to the *C. parapsilosis* species complex, *C. tropicalis*, *C. albicans*, and *C. dubliniensis*. MIC testing found that it demonstrated low MICs to azoles and amphotericin B.

Candida auris was first reported from Japan and South Korea from external ear samples in patients with chronic otitis media. At the time, its clinical significance was unclear. In 2011, this species was detected in South Korea as an agent of bloodstream infection in three patients, all of whom had pre-existing clinical conditions and were receiving broad-spectrum antibiotics and parenteral nutrition [23]. The isolates were originally misidentified using phenotypic methods as either *Candida haemulonii* or *Rhodotorula glutinis*, and DNA sequencing was required to provide the final identification. This species showed a close relationship to *Candida haemulonii* when studied phylogenetically. The MIC to fluconazole was high (range 2 to 128 μg/mL), but all isolates had low MICs to echinocandin drugs. All patients demonstrated persistent fungemia (10–31 days) that ultimately resolved with catheter removal and replacement of fluconazole therapy with amphotericin B.

Basidiomycetous Yeast

Cryptococcus Species

The two major species causing human infection are *Cryptococcus neoformans* and *Cryptococcus gattii*. After historically recognizing them as the single species *C. neoformans*, a number of phylogenetic studies have now resulted in their designation as separate species [24]. Most commercial yeast identification systems as well as the common cryptococcal antigen test performed on blood and spinal fluid do not distinguish between the two species. CGB (glycine-canavanine-bromthymol blue) medium is now commercially available in the United States to separate isolates into the two species, relying on the ability of *C. gattii* strains to assimilate glycine in the presence of canavanine and turn the medium from green to cobalt blue. *C. neoformans* strains do not assimilate glycine and the medium remains green after two to five days of incubation [25]. A variety of molecular methods can also be used to separate the two species, including MLST (multilocus sequence typing) and AFLP (amplified fragment length polymorphism) [26•]. A consensus MLST scheme for subtyping cryptococcal strains has been published [27].

The species *Cryptococcus neoformans* comprises organisms of serotypes A (*C. neoformans* var. *grubii*), D (*C. neoformans* var. *neoformans*) and AD (aneuploid hybrid strains). They are best known as causes of pneumonia, fungemia and meningitis in individuals world-wide, primarily in HIV-infected hosts but also in organ transplant recipients and individuals taking TNF-inhibitors for treatment of rheumatoid arthritis. Serotype A is the most commonly isolated type worldwide. Serotype D is more geographically restricted, found mostly in Mediterranean Europe. Hybrids of serotypes A and D are occasionally found in human disease.

Cryptococcus gattii refers to serotype B and C organisms, and may also be a species complex [24, 28]. This species has been found in Africa causing fungemia and meningitis in HIV-infected individuals, with a clinical presentation indistinguishable from that of serotype

A disease. In the 1980s and 90s, cases of *C. gattii* were also reported in otherwise healthy individuals in Australia, as well as from Southern California and South America. In 1999, *C. gattii* appeared in Vancouver Island, Canada, causing disease in both humans and animals [reviewed in 29]. This disease was traced to a particular molecular type, VGII, which is genetically different from types found in Australia (mostly VGI). *C. gattii* has also surfaced in the northwestern United States (Washington, Oregon, Idaho, California). Outbreak strains (VGIIa, VGIIb, and VGIIc) differ from non-outbreak strains (VGI, VGIII, and VGIV) in clinical presentation and patient characteristics. Patients with outbreak strains were more likely than patients with non-outbreak strains to have pre-existing medical conditions and respiratory symptoms, and less likely to have central nervous system symptoms [30•]. In another study, fluconazole MIC values were found to be correlated with subtype. VGI and VGIII isolates had comparatively low MIC to fluconazole, while VGIIc isolates had high MICs (16–32 μg/mL) to this drug [31, 32]. It is not clear if these differences translate into variation in responsiveness of the *C. gattii* subtypes to fluconazole therapy.

A number of *Cryptococcus* species that are not *C. neoformans* or *C. gattii* have been implicated in human disease. It is difficult to evaluate such reports because in most cases the isolates were not confirmed using DNA sequencing or other molecular testing, so the possibility of misidentification was not always formally ruled out.

Trichosporon Species

Members of the genus *Trichosporon* are increasingly recognized as causes of serious human disease, as well as skin and hair infections. A recent review regards this genus as the second most important cause of disseminated yeast infections in immunosuppressed patient populations [33], but it may fall to third if both *Cryptococcus* and *Candida* are counted. Although 37 species of *Trichosporon* are considered valid at this writing, nearly all systemic human infections area caused by one of six species, including *T. asahii*, *T. asteroides*, *T. cutaneum*, *T. inkin*, *T. mucoides*, and *T. ovoides*. The former *Trichosporon beigelii* has been declared an invalid name and is no longer used. Some of the newly reported species include *Trichosporon mycotoxinivorans*, an agent causing pneumonia in a cystic fibrosis patient [34].

Although it is fairly straightforward to identify *Trichosporon* to the genus level using phenotypic features, members of *Trichosporon* can be confused with the genera *Blastoschizomyces* and *Geotrichum* when morphology alone is considered. It is important to appreciate that *Trichosporon* and *Blastoschizomyces/Geotrichum* can both display arthroconidia on morphology media. Urease is important in distinguishing *Trichosporon* (urease-positive) from *Blastoschizomyces/Geotrichum* (urease-negative). DNA sequencing is mandatory to identify the individual species of *Trichosporon*. The ribosomal IGS (intergenic spacer) region is the preferred region to target in distinguishing species from one another, as the ITS region does not have sufficient discriminatory power. In addition, nine *T. asahii* genotypes can be distinguished based on analysis of the IGS region [33].

Treatment of trichosporonosis remains challenging. Strains of various species resistant to amphotericin B, fluconazole, and itraconazole have been reported. Echinocandins are not recommended for treating *Trichosporon* infections due to low activity. Combination therapy

with amphotericin B and an azole drug may be the most reliable avenue for successful treatment.

Rhodotorula Species

Most clinically important members of this genus are either *Rhodotorula mucilaginosa* or *Rhodotorula glutinis*. These organisms are easily distinguished by their orange-pink color and lack of pseudohyphae. *Rhodotorula* is a normal inhabitant of moist skin and can be recovered from bathrooms, showers, and toothbrushes. It is an uncommon cause of meningitis, fungemia, endocarditis, and other systemic infections in immunocompromised patients. In a recent 12-year review of bloodstream infections at a referral cancer center, 21 cases of *Rhodotorula* infections were reported [35]. *Rhodotorula* infections can be difficult to treat due to both azole and echinocandin resistance, but are generally responsive to amphotericin B.

Malassezia Species

The taxonomy of *Malassezia* remains a topic of much investigation. The Mycobank database lists 17 species at this writing. *Malassezia* species are considered part of the normal skin flora in humans and animals. They can cause superficial infection known as pityriasis versicolor as well as fungemia and other deep infections in infants and adults [36]. *M. pachydermatis* is the best recognized, probably because it can grow on fungal media without lipid supplementation.

Conclusions

Advances in identification and taxonomy of yeast have led to the recognition of many novel “cryptic species” or “species complexes” that are mostly refractory to the traditional phenotype-based identification methods commonly employed in clinical laboratories. Furthermore, continued increases in susceptible patients and the selection pressures imposed by antifungal drug use will continue to result in the appearance of novel organisms that may not be easily recognized in clinical laboratories. Precise naming of such agents will require the use of DNA or MALDI-based identification methods. DNA-based methods are preferred for identification of unknown agents because, although their DNA sequence will not match precisely any sequences in published databases, their closest genetic neighbors can be easily determined, facilitating their taxonomic placement. As such instrumentation becomes more affordable molecular methods will probably be used more and more frequently, especially in reference institutions and those serving large numbers of critically ill patients. However, at this time such precise levels of identification may not be required for most sporadic yeast isolates. Identification as “*Candida* X species complex” may become the norm. It will be important for clinicians to appreciate that identification at the species complex level may encompass multiple species, not all of which may share the same antifungal drug susceptibility profile.

The clinical value of routinely identifying and reporting cryptic species is not clear at this time. A major reason for precise species identification is the central role of species identification in predicting antifungal resistance for yeasts that have not been specifically

tested for susceptibility. With the adoption of species-specific MIC breakpoints, it will be mandatory to identify a given yeast isolate to species prior to reporting an MIC profile, so that the correct breakpoints can be applied. However, an association between species and antifungal susceptibility/resistance has not been fully delineated for many of the cryptic species. For example, *Candida nivariensis* has been noted as uniformly resistant to multiple azole drugs, but *Candida bracarensis* shows more variable susceptibility. It would probably be worthwhile to distinguish *C. nivariensis* from *C. glabrata*, but the value of routinely distinguishing *C. bracarensis* from *C. nivariensis* is less clear.

Finally, the end of “one fungus-two names” nomenclature rules will hopefully provide important clarity to the identification of fungal pathogens in the clinical laboratory, by allowing one name to be consistently used for human pathogenic yeasts. Further studies will be required to assess the epidemiology and significance of these taxonomic changes on clinical practice and patient management.

Acknowledgments

The findings and conclusions in this presentation/report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

References

Papers of particular interest, published recently, have been highlighted as:

• Of importance

•• Of major importance

1. van Belkum A, et al. Biomedical mass spectrometry in today’s and tomorrow’s clinical microbiology laboratory. J Clin Microbiol. 2012; 50:1513–1517. [PubMed: 22357505]
2. Taylor JW, et al. Phylogenetic species recognition and species concepts in fungi. Fungal Genet Biol. 2000; 31:21–32. [PubMed: 11118132] This paper describes the rationale behind the concept of a phylogenetic species.
3. Hawksworth DL. Pandora’s mycological box: molecular sequences vs. morphology in understanding fungal relationships and biodiversity. Rev Iberoam Micol. 2006; 23:127–133. [PubMed: 17196017]
4. Clinical and Laboratory Standards Institute. MM18-A: Interpretive criteria for identification of bacteria and fungi by DNA target sequencing; Approved Guideline. 2007WayneCLSI Lists the DNA targets currently used to identify most common fungal species.
5. Hawksworth DL. Managing and coping with names of pleomorphic fungi in a period of transition. Mycosphere. 2012; 3:52–64. Explains the rationale behind the end of the “one fungus-two names” taxonomic rule.
6. Miceli MH, Diaz JA, Lee SA. Emerging opportunistic yeast infections. Lancet Infect Dis. 2011; 11:142–151. [PubMed: 21272794]
7. Schmid J, et al. Increased mortality in young candidemia patients associated with presence of a *Candida albicans* general-purpose genotyp. J Clin Microbiol. 2011; 49:3250–3256. [PubMed: 21775553]
8. Ells R, Kock JLF, Pohl CH. *Candida albicans* or *Candida dubliniensis*? Mycoses. 2011; 54:1–16. [PubMed: 19682314]
9. Lockhart SR. Do hospital microbiology laboratories still need to distinguish *Candida albicans* from *Candida dubliniensis*? J Clin Microbiol. 2011; 49:4415. [PubMed: 21998427]

10. Romeo O, Criseo G. *Candida africana* and its closest relatives. Mycoses. 2011; 54:475–486. [PubMed: 20667001]
11. Falagas ME, Roussos N, Vardakas KZ. Relative frequency of *albicans* and the various non-*albicans Candida* species among candidemia isolates form inpatients in various parts of the world: a systematic review. Int J Infect Dis. 2010; 14:e954–e966. [PubMed: 20797887]
12. Warren TA, et al. *Candida bracarensis* bloodstream infection in an immunocompromised patient. J Clin Microbiol. 2010; 48:4677–4679. [PubMed: 20881164]
13. Yang YL, et al. Comparison of human and soil *Candida tropicalis* isolates with reduced susceptibility to fluconazole. Plos One. 2012; 7:e34609. [PubMed: 22496832]
14. Kurtzman CP, Fell JW, Boekhout T. The yeasts: a taxonomic study (5th ed.). 2011LondonElsevier The standard manual for yeast taxonomy and identification.
15. Savini V, et al. What do we know about *Candida guilliermondii*? A voyage throughout past and current literature about this emerging yeast. Mycoses. 2011; 54:434–441. [PubMed: 21039941]
16. Jensen RH, Arendrup MC. *Candida palmioleophila*: characterization of a previously overlooked pathogen and its unique susceptibility profile in comparison with five related species. J Clin Microbiol. 2011; 49:549–556. [PubMed: 21147953]
17. Paredes K, et al. Molecular identification and antifungal susceptibility of clinical isolates of *Candida rugosa* species complex and proposal of the new species *Candida neorugosa*. J Clin Microbiol. 2012
18. Taverna CG, et al. First case report of bloodstream infection due to a Candida species closely related to the novel species *Candida pseudorugosa*. J Clin Microbiol. 2012; 50:2165–2169. [PubMed: 22461681]
19. Kurtzman CP. Phylogeny of the ascomycetous yeasts and the renaming of *Pichia anomala* to *Wickerhamomyces anomalus*. Antonie van Leeuwenhoek. 2011; 99:13–23. [PubMed: 20838888]
20. Al-Sweih N, et al. *Kodamaea ohmeri* as an emerging pathogen: a case report and review of the literature. Med Mycol. 2011; 49:766–770. [PubMed: 21438792]
21. Pfüller R, et al. A novel flucytosine-resistant yeast species, *Candida pseudoaaseri*, causes disease in a cancer patient. J Clin Microbiol. 2011; 49:4195–4202. [PubMed: 21976765]
22. Adam H, et al. Identification of a new species, *Candida subhashii*, as a cause of peritonitis. Med Mycol. 2009; 47:305–311. [PubMed: 18798116]
23. Lee WG, et al. First three reported cases of nosocomial fungemia caused by *Candida auris*. J Clin Microbiol. 2011; 49:3139–3142. [PubMed: 21715586]
24. Bovers M, Hagen F, Boekhout T. Diversity of the *Cryptococcus neoformans-Cryptococcus gattii* species complex. Rev Iberoam Micol. 2008; 25:S4–S12. [PubMed: 18338917]
25. Kwon-Chung KJ, Polacheck I, Bennett JE. Improved diagnostic medium for separation of *Cryptococcus neoformans* var. *neoformans* (serotypes A and D) and *Cryptococcus neoformans* var. *gattii* (serotypes B and C). J Clin Microbiol. 1982; 15:535–537. [PubMed: 7042750]
26. McTaggart L, et al. Rapid identification of *Cryptococcus neoformans* var. *grubii*, *C. neoformans* var. *neoformans*, and *C. gattii* by use of rapid biochemical tests, differential media, and DNA sequencing. J Clin Microbiol. 2011; 49:2522–2527. [PubMed: 21593254] A very helpful description of the most recent ways to separate these two species.
27. Meyer W, et al. Consensusmulti-locus typing scheme for *Cryptococcus neoformans* and *Cryptococcus gattii*. Med Mycol. 2009; 47:561–570. [PubMed: 19462334]
28. Ngamskulrungroj F, et al. Genetic diversity of the *Cryptococcus* species complex suggests that *Cryptococcus gattii* deserves to have varieties. PLoS One. 2009; 4:e5862. [PubMed: 19517012]
29. Byrnes EJ, et al. *Cryptococcus gattii*: an emerging fungal pathogen infecting humans and animals. Microbes Infect. 2011; 13:895–907. [PubMed: 21684347]
30. Harris J, et al. *Cryptococcus gattii* in the United States: clinical aspects of infection with an emerging pathogen. Clin Infect Dis. 2011; 53:1188–1195. [PubMed: 22016503] Describes clinical aspects of patients diagnosed with C. gattii infection.
31. Iqbal N, et al. Correlation of genotype and in vitro susceptibilities of *Cryptococcus gattii* strains from the Pacific Northwest of the United States. J Clin Microbiol. 2010; 48:539–544. [PubMed: 20007380]

32. Lockhart SR, et al. Epidemiologic cutoff values for triazole drugs in *Cryptococcus gattii*: correlation of molecular type and in vitro susceptibility. Diagn Microbiol Infect Dis. 2012

33. Chagas-Neto TC, Chaves GM, Colombo AL. Update on the genus *Trichosporon*. Mycopathologia. 2008; 166:121–132. [PubMed: 18568419]

34. Hickey PW, et al. *Trichosporon mycotoxinivorans*, a novel respiratory pathogen in patients with cystic fibrosis. J Clin Microbiol. 2009; 47:3091–3097. [PubMed: 19656976]

35. Chitasombat MN, et al. Rare opportunistic (non-*Candida*, non-*Cryptococcus*) yeast bloodstream infections in patients with cancer. J Infect. 2012; 64:68–75. [PubMed: 22101079]

36. Gaitanis G, et al. The *Malassezia* genus in skin and systemic diseases. Clin Microbiol Rev. 2012; 25:106–141. [PubMed: 22232373]

Table 1

Anamorph, teleomorph and older names for selected human pathogenic yeast

Anamorph name	Teleomorph name (if present)	Older name
Blastoschizomyces capitatus	*Dipodascus capitatus*	*Geotrichum capitatum*
Candida ciferrii	*Trichomonoascus ciferrii*	*Stephanoascus ciferrii*
Candida famata	*Debaryomyces hansenii*	
Candida fermentati	*Meyerozyma caribbica*	*Pichia caribbica*
Candida guilliermondii	*Meyerozyma guilliermondii*	*Pichia guilliermondii*
Candida guilliermondii var. *membranifaciens*	*Kodamaea ohmeri*	*Pichia ohmeri*
Candida kefyr	*Kluyveromyces marxianus*	
Candida krusei	*Pichia kudriavzevii*	*Issatchenkia orientalis*
Candida lipolytica	*Yarrowia lipolytica*	
Candida lusitaniae	*Clavispora lusitaniae*	
Candida palmioleophila	None	
Candida pelliculosa	*Wickerhamomyces anomalus*	*Pichia anomala*
		Hansenula anomala
Candida utilis	*Lindnera jadinii*	
Cryptococcus gattii	*Filobasidiella bacillispora*	*Cryptococcus neoformans* var. *gattii*
Cryptococcus neoformans	*Filobasidiella neoformans*	*Cryptococcus neoformans* var. *grubii* (serotype A) and *C. neoformans* var. *neoformans* (serotype D)